POWER1 – A Double-Blind, Randomized, Multicenter Phase 2/3 Study Evaluating the Efficacy and Safety of Vormatrigine in Adults with Focal Onset Seizures

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BACKGROUND

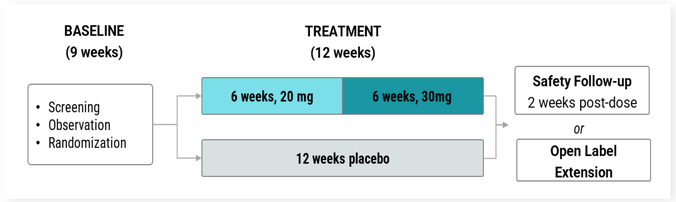
- There are ~50 million individuals worldwide living with epilepsy, the majority of whom have focal epilepsy.
- Focal onset seizures (FOS) are characterized by localized neuronal hyperexcitability, with current standard-of-care limited by tolerability issues and need for titration to avoid side effects.
- Vormatrigine, a functional state modulator that selectively targets the hyperexcitable state of CNS sodium channels, is currently in development for adult FOS and generalized epilepsy.
- Recent data highlight a superior preclinical and early clinical profile compared to currently approved antiseizure medications (ASMs), demonstrate a favorable safety and tolerability profile in doses up to 45 mg, with no clinically significant food effect.
- Notably, emerging data demonstrate vormatrigine's ability to significantly exceed therapeutic concentrations while being well tolerated, without the need for titration.

➢ ***POWER1 is a global, multicenter, double-blind, randomized, parallel design Phase 2/3 registrational study evaluating the efficacy, safety, and pharmacokinetics of vormatrigine in adults with FOS.***

METHODS

POWER1 Study Design

- POWER1 (NCT06999902) is a global, multicenter, double-blind, randomized, parallel design Phase 2/3 study enrolling ≈230 participants aged 18-75 years with FOS, currently taking 1-3 ASMs.
- Participants are randomized 1:1 to receive vormatrigine QD, at 20mg for the first 6 weeks and 30 mg for the second 6 weeks, or matching placebo for 12 weeks.
- The study will consist of Screening/Observation (Baseline), Treatment and Follow-up periods.
- Participants will have the option to continue study treatment in an open-label extension (OLE) study.



PRIMARY ENDPOINT

- Median percent change in monthly (28 days) focal seizure frequency from Baseline Period to Treatment Period

KEY SECONDARY ENDPOINTS

- Proportion of subjects experiencing a ≥50% reduction in monthly (28 days) focal seizure frequency from Baseline Period to Treatment Period
- Percent change in monthly focal seizure frequency from Baseline Period to the Treatment Period

POWER1 Study Design and Endpoints. Further secondary and exploratory endpoints will examine the effect of vormatrigine on additional efficacy and safety and tolerability outcomes.

PARTICIPANT ELIGIBILITY

POWER1 Study Eligibility

KEY INCLUSION CRITERIA

- A diagnosis of focal onset epilepsy according to International League Against Epilepsy (ILAE) Classification (2017), and progressive epilepsy cause ruled out on CT or MRI
- Male or female aged 18-75 years inclusive
- On 1–3 stable doses of ASMs for at least 4 weeks prior to screening

KEY EXCLUSION CRITERIA

- Planned or recent epilepsy surgery or recent neurostimulator placement
- Pseudo- or psychogenic seizures, uncountable cluster seizures only or episode of convulsive status requiring hospitalization/intubation in the past 12 months
- History of schizophrenia, obsessive-compulsive disorder, or other serious mental health disorders
- Significant cardiac conduction abnormalities or family history of sudden death
- Use of prohibited drugs
- Pregnant or breastfeeding at the time of Screening, positive serum pregnancy test at Screening or planning to become pregnant within 14 days of the last study drug dose

VORMATRIGINE POWER STUDIES: PATIENT-CENTERED DESIGN

Decentralized Study Design Customized to Meet Patient Needs

❖ **Designed with patients' needs in mind**
❖ **Patients may complete study visits from home**
❖ **Streamlined at-home nurse services**
❖ **Increased access for potential patients normally excluded**

POWER2 Phase 3 Study Design

- Global, multicenter, double-blind, placebo-controlled, 12-week study
- Option to continue treatment in an open-label extension study (up to 2 years)

Dosing

- Vormatrigine 40 mg, 30 mg, 20 mg, or placebo QD for 12 weeks

Key Eligibility Criteria

- Adults aged 18-85 years with FOS, currently on 1-3 concomitant ASMs

Primary Endpoint

- Percent change in monthly focal seizure frequency

POWER1 RECRUITMENT COMPLETE – POWER2 NOW ENROLLING

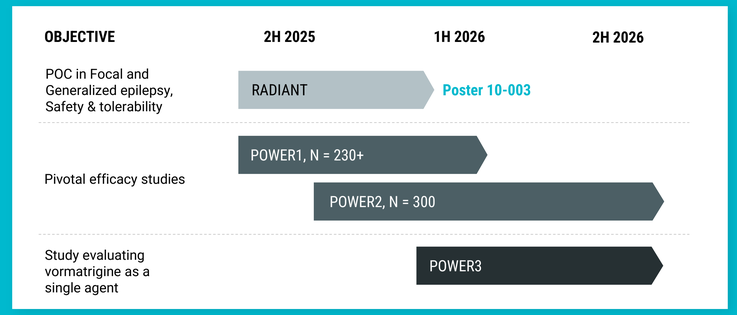
Healthcare Providers Can Help Their Patients See If They Qualify for POWER2, the Second Registrational Study in FOS, by Referring Them to the Online Pre-Screener at energyepilepsystudies.com/power2

power1 — **Recruitment Complete**

power2 — **Now Enrolling**

VORMATRIGINE ENERGY PROGRAM

- **Expanding on preclinical and preliminary clinical data, including the recent positive RADIANT study results, the POWER1 study will examine the efficacy, safety and pharmacokinetics of vormatrigine as a potential best-in-class precision ASM for FOS.**
- **Recruitment completed for POWER1, with topline results expected in 1H 2026.**
- **POWER2 study started, with enrollment expected to complete in 2H 2026 and topline results expected in 2027.**



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